UNITED STATES OF AMERICA

BEFORE THE

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

PETITION OF ENVIRONMENTAL DEFENSE FUND, INC.
AND NATURAL RESOURCES DEFENSE COUNCIL, INC.
TO THE SECRETARY OF HEALTH, EDUCATION AND WELFARE
TO HOLD HEARINGS AND PROMULGATE REGULATIONS UNDER
THE PUBLIC HEALTH SERVICE ACT GOVERNING RECOMBINANT
DNA ACTIVITIES

The Environmental Defense Fund (EDF) and the Natural Resources Defense Council (NRDC) hereby petition the Secretary of Health, Education and Welfare (hereafter "the Secretary") under the authority granted him by §361 of the Public Health Services Act (42 U.S.C. §264) to hold public hearings and promulgate regulations governing recombinant DNA[1/] research and technology in which fragments of DNA from different organisms, cells or viruses are combined in novel ways and introduced into a living host organism or cell.

1/ DNA - deoxyribonucleic acid, the chemical substance which contains all genetic information.

Recombinant DNA technology permits the creation of organisms or viruses with an unprecedented genetic make-up which may have the potential of causing grave and irreversible harm to humans and the environment. The extent of our current knowledge does not allow us to predict all of the possible results of experiments involving the manipulation of genes. Because most of the present and proposed recombinant DNA research and technology involves the genetic modification of bacteria or viruses, there exists the potential danger of creating a highly deleterious communicable infectious agent that could be introduced into and spread among laboratory workers and/or the general population (see infra, pp. 9 - 12).

Recognizing the potential hazards inherent in recombinant DNA research, the National Institutes of Health (hereinafter "NIH") on 23 June, 1976 promulgated guidelines [1/] which prohibit certain experiments where the potential risks to human health are deemed to be particularly high, and require a graded set of safety procedures for all other experiments (see 41 Fed. Reg. No. 131, part II, pp. 27902-27943, July 7, 1976). NIH also filed a draft environmental impact statement (hereinafter the "impact statement") on 1 September, 1976, which sets forth some of the possible dangers of recombinant DNA research and technology (see 41 Fed. Reg. No. 176, pp. 38425-44, Sept. 9, 1976). NIH indicated that the guidelines are not a final statement of public policy on

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[1/] The petitioners take no position at this time concerning the adequacy of the safety standards set forth in these guidelines.

recombinant DNA research and technology but rather the beginning of full public consideration of all relevant issues.

The guidelines apply only to recombinant DNA research supported by the NIH. While Dr. Donald Fredrickson, the director of NIH, has called on all government agencies and "all who support or conduct such research throughout the United States" (41 Fed. Reg. No. 131, p. 27906, July 7, 1976) to voluntarily adopt the NIH guidelines, only the National Science Foundation, Department of Defense, and the Energy Research and Development Administration have formally done so.* Therefore, a significant portion of recombinant DNA research and technology is not covered by any mandatory set of safety procedures, leaving the public unprotected from its potential hazards. Furthermore, it is the position of the petitioners that the public did not have an adequate opportunity to participate in the basic policy decisions underlying the NIH Guidelines.

For these reasons, EDF and NRDC request that: (1) a public hearing of broader scope than those held this year at NIH be held on the questions of to what extent and under what conditions recombinant DNA research and technology should be allowed to proceed; (2) final regulations be promulgated based on the record of that hearing which would apply to all recombinant DNA research and technology in the

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* Dr. Joe Perpich, National Institutes of Health, personal communication.

United States; and (3) the present NIH guidelines be promulgated immediately as interim relief regulations governing all parties conducting or supporting such research.

This document includes:

I. Scope of the Petition

By this petition EDF and NRDC seek interim and final regulations which will protect the public from the potential hazards of uncontrolled recombinant DNA research and technology.

In this petition the term "recombinant DNA research and technology" means all procedures in which DNA fragments from two or more different organisms or viruses which do not normally recombine in nature are recombined in the laboratory and inserted into a living host cell or organism in such a way as to alter its genetic make-up. This includes, but is not limited to, any experiments involving transportation of or commercial use of recombinant

DNA molecules or the products derived therefrom. NRDC and EDF seek regulations governing all recombinant DNA research and technology including, but not limited to:

(a) All experiments discussed in the "Guidelines for Research Involving Recombinant DNA Molecules" issued by the National Institutes of Health on June 23, 1976 and published in the Federal Register Part II on July 7, 1976;

(b) All experiments in which chemically or enzymatically synthesized DNA is inserted into a living host, plasmid or virus; and

(c) All other procedures in which DNA from any two sources which do not normally exchange genetic information may function within the same cell.

NRDC and EDF seek regulations which would cover all persons and organizations conducting or supporting recombinant DNA research including, but not limited to:

1. Recipients of Research grants awarded by any agency within the Department of Health, Education and Welfare;

2. Private corporations;

3. Private and public universities; and

4. Other departments and agencies of the Federal Government.

II. Petitioners

Petitioner Environmental Defense Fund, Inc., is a not-for-profit public-benefit membership corporation organized and existing under the laws of the State of New York. Its principal office and place of business is located at 162 Old Town Road, East Setauket, New York. It also maintains offices in Washington, D.C.; New York, New York; Denver, Colorado; and Berkeley, California. EDF has a nationwide membership of over 40,000 persons, composed of scientists, educators, lawyers, and other citizens dedicated to the protection of the environment and the wise use of natural resources. Many of these persons and their children will be subjected to the increased risk of adverse health effects discussed in at pp. 9 - 12, infra, if the Secretary does not adopt effective regulations controlling the relevant procedures. By its activities, EDF seeks the preservation and restoration of environmental quality and the protection of the country's natural resources on behalf of the general public. Its objectives include combining "the best scientific findings with the most appropriate social action discovered by the social sciences and legal theory in order that practical decisions shall be made which shall best promote a quality environment." (EDF By-laws, Art. 1:2(d)).

Petitioner Natural Resources Defense Council, Inc., is a not-for-profit, tax-exempt corporation organized under the laws of the State of New York, with offices at 15 West 44th Street, New York, New York; 917 15th Street, N.W., Washington, D.C.; and 2345 Yale Street, Palo Alto, California. NRDC is a national organization dedicated to environmental protection, including

protection of the human environment. NRDC has 24,000 members and contributors in the United States. Many of these persons and their children will be subjected to the increased risk of adverse health effects discussed in pp. 9 - 12, infra, if the Secretary does not adopt effective regulations controlling the relevant procedures. Among the methods NRDC uses to achieve its objectives are: (1) improving federal agency decision-making which affects the environment by commenting, furnishing information, participating in administrative proceedings, and bringing lawsuits where legal duties are not being fulfilled; and (2) improving federal agency decision-making which affects the environment by encouraging agencies to solicit and utilize the views, knowledge, and expertise of members of the general public.

III. The Need to Control Recombinant DNA Research and Technology in the Interest of Public Health

The techniques defined above enable scientists to recombine the DNA from two unrelated species and, thus, construct organisms which may express genes from biologically unrelated sources. Because the properties of such deliberately or accidentally constructed organisms are unknown and may represent hitherto nonexistent hazards both to human health and the ecology, members of the scientific community have raised the questions of whether or not proceeding with this type of research at this time is prudent, and, if so, whether or not the public and the environment can be adequately protected

from potentially hazardous novel organisms which might arise from such research.

Addressing these questions, NIH formed a committee (the Recombinant DNA Molecule Program Advisory Committee) composed of scientists, many of whom were directly involved in recombinant DNA research, to draft guidelines governing the conduct of recombinant DNA research and establish safeguards to protect the public and the environment from potential hazards. The guidelines, applying only to NIH supported research, were made public June 23, 1976. Recognizing the far-reaching environmental consequences which could result if infectious or otherwise dangerous organisms able to compete successfully with existing organisms were to be produced by recombinant DNA research, and in response to requests from the public, NIH prepared a Draft Environmental Impact Statement which was released September 1, 1976.

The Impact Statement, in discussing the alternative of "no action," unambiguously concludes that regulation of recombinant DNA research and technology is essential for the protection of the public:

> "the 'no action' alternative would greatly increase the probability that possible hazardous organisms would be released into the environment. . . . It is concluded that the 'no action' alternative would not afford adequate protection of laboratory workers, the general public, and the environment from the possible hazards described in section IV-C-1." (at p. 48).

Some of the possible hazards which could arise either directly or as an inadvertent result of recombinant DNA research are discussed in Section IV-C of the Impact Statement. One may

expand this list to include additional untoward health effects. The following are examples of potential threats to human health which could result from recombinant DNA research and technology:

1. Most of the proposed and ongoing recombinant DNA research involves strains of the bacterium Escherichia coli (E. coli) as a host for plasmids containing DNA from other sources. E. coli is a common resident of the human colon, is responsible for nearly 100% of human upper urinary tract infections[1/] and for approximately 30-40% of the cases of sepsis[2/] (infection of the human bloodstream), which is often fatal. While the strains of E. coli used in recombinant DNA research (variants of strain K-12) do not normally colonize the human colon, they can under unusual conditions, particularly in patients weakened by another disease state. Perhaps more serious, however, is the capacity of K-12 strains of E. coli to exchange DNA with other similar or related organisms.[3/] Genetic exchange between E. coli and strains of Salmonella,[4/] a human pathogen, is well documented. Since the genetic determinants in infectivity and virulence of bacteria are not understood, one must consider the possibility that even a seemingly trivial modification of the E. coli genome might greatly alter its capacity for infection and propagation within humans.

1/ B. D. Davis, et al., Microbiology 768 (2nd ed. 1973).

2/ Dr. Halsted Holman - Oral testimony before a hearing of the Subcommittee on Health of the Senate Committee on Labor and Public Welfare, Sept. 22, 1976

3/ Davis, et al., supra at 182-200.

4/ Id. at 194.

In view of the ubiquitous nature of E. coli, the fact that all strains including K-12 already have the capacity for human infection, and E. coli's ability to exchange genetic material with other bacteria, the deliberate genetic modification of even "weakened" strains of E. coli poses a potentially serious threat to human health.

2. DNA can be taken from organisms that produce toxins (e.g. botulinum) creating the possibility that the host organism, which occupies a different ecological niche, will acquire the ability to produce the toxin. This would be particularly serious if such genes were expressed in strains of E. coli capable of colonizing the human colon.

3. Genes which code for resistance to antibiotics are transferred by some recombinant DNA experiments to strains of bacteria that were not previously resistant.

4. The animal virus on which the most genetic information is available is simian virus 40 (SV-40), which produces tumors in some animals and infects humans, although apparently with no pathological symptoms. However, the genetic basis for the virus causing tumors in monkeys but not humans is not understood. Therefore, the possibility exists that even an apparently innocuous modification of SV-40 DNA could render the virus tumorigenic or otherwise pathogenic to humans, thus creating a serious hazard to human health. Yet it is SV-40, and polyoma

virus, which also produces tumors in animals, which are the primary objects of recombinant DNA research in animal viruses.

5. The virulence of influenza virus, and the spontaneous occurrence in nature at certain times of devastating flu epidemics (such as the one of 1918) is apparently controlled by the reassortment in nature of the 12 subunits of the viral RNA[1/]. Yet the genetic basis and the mechanism by which these viruses are rendered highly virulent is not understood. Again, therefore, any recombinant DNA procedure involving any animal virus or cells containing such a virus must be considered to pose the risk of creating highly virulent or infectious strains.

6. The expression of <u>any</u> foreign gene, however seemingly innocuous it may be in the cells of a human or other mammal, whether inserted by viral infection or some other mechanism, poses the risk that a protein will be produced in the infected cells which has never been seen by the host's immune system. Thus the possibility of an auto immune disease exists (as in rheumatic fever or degenerative kidney disease) in which the body produces antibodies against proteins within or produced by its own cells, ultimately destroying the cells themselves. The NIH guidelines discuss "harmful" genes in the sense of DNA specifying antibiotic resistance factors or protein toxins.

1/ Davis, et al., <u>supra</u> at 1318. RNA = ribonucleic acid. Some viruses contain RNA rather than DNA.

In the context of auto-immune disease, however, the gene specifying any foreign protein must be considered potentially harmful.

7. The expression of even a "normal" metabolic enzyme in human, animal or plant cells which was not under the control of the cell's normal complex regulatory mechanism, could lead to severe metabolic disruptions and an ensuing disease state, similar to existing cases of metabolic disease where the defect is in a regulatory gene, rather than once coding for a specific enzyme.

Both the NIH guidelines and the Impact Statement recognize that humans harboring or infected by bacteria or viruses containing recombinant DNA may, under certain conditions, suffer a variety of serious adverse health effects. If such modified bacterial or viral agents can survive and propagate outside the laboratory and thus produce new identical organisms capable of producing infection and/or toxic effects on human beings, there exists the potential for a "communicable disease" within the meaning of Section 361 of the Public Health Service Act (42 U.S.C. §264) (see Section II above). Because some of the organisms created by recombinant DNA research have never existed before, the health and environmental effects of such novel microorganisms are inherently unpredictable. Nevertheless, the danger of the creation of a potentially serious communicable disease organism makes it incumbent upon the Department of Health, Education and Welfare to exercise its statutory authority and take whatever regulatory measures are necessary to protect the public health.

While EDF and NRDC commend the monumental effort made by NIH to regulate this potentially hazardous branch of research within its own jurisdiction, we are disturbed by the fact that the guidelines cover only NIH supported research, leaving large segments of the scientific and industrial communities subject to no required safety procedures. Recombinant DNA research and technology is now being pursued and supported by private corporations, agencies of the Federal government, as well as scientists at universities and private institutions.

General Electric is trying to develop a bacteria which can degrade petroleum and could be used to consume oil spills. Imperial Chemical Industries Ltd. (ICI) of Britain is trying to develop a virus which produces insulin. (Janice Crossland, "Hands on the Code", Environment 18:6, September 1976). The drug industry in the United States has also expressed interest in the commercial use of recombinant DNA techniques. Federal agencies such as the Department of Defense may contemplate conducting experiments. Scientists at universities whether they receive government grants or not are conducting recombinant DNA research. Therefore, we consider a uniform set of regulations covering all parties engaging in recombinant DNA research to be absolutely necessary.

IV. The Secretary of HEW Has the Authority To Regulate All Recombinant DNA Activities

Section 361 of the Public Health Services Act (42 U.S.C. §264) gives the Secretary of Health, Education and Welfare the authority to regulate all recombinant DNA research and technology. The Section empowers the Secretary to:

> ". . . make and enforce such regulations as in his judgement are necessary to prevent the introduction, transmission, or spread of communicable

diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession . . ."

It further provides that:

for purposes of carrying out and enforcing such regulations, the [Secretary] may provide for such inspection, . . . disinfection . . . and other measures, as in his judgment may be necessary.

Recombinant DNA research and technology could create novel infectious agents or increase the virulence and range of existing infectious agents. The Draft Environmental Impact Statement recognizes that recombinant DNA activities could produce microorganisms that cause disease in laboratory workers and the general public. In describing the Guidelines the Draft EIS states:

"The emphasis on protection of laboratory workers from infection reflects the fact that laboratory workers are the persons at the greatest risk of infection and that the most likely route of escape of possibly hazardous agents from the laboratory is the laboratory worker." (41 Fed. Reg. 38432)

In describing the highest level of physical containment required by the Guidelines to the Draft EIS states that such facilities are:

"designed to contain microorganisms that are extremely hazardous to man or may cause serious epidemic disease."

The kinds of disease which may be caused by recombinant DNA activities are described in Section III of this petition (infra at pp. 9 - 12).

The Secretary has defined "communicable disease" in regulations promulgated under Section 361 to govern the importation of animals and establish drinking water standards. For the purposes of both these sets of regulations a communicable disease is "An illness due to an infectious agent or its toxic product . . ." transmitted by persons, animals, plants or the inanimate environment. (42 C.F.R. §§71.1(b), 72.1(b)). These regulatory definitions of communicable

disease illustrate that the Secretary has the authority under §361 to regulate infectious agents from any source, transmitted by any means.

Because microorganisms produced by recombinant DNA activities may spread disease among humans, it has already been recognized that regulations promulgated pursuant to authority under §361 control transportation of DNA materials. Section II-C of the NIH Guidelines (41 Fed. Reg. 27914) states that the shipment of recombinant DNA materials is governed by 42 C.F.R. §72.25 which specifies safety requirements for the transportation of etiologic agents.[1/] An "etiologic agent" is defined as ". . . a viable micro-organism or its toxin which causes, or may cause, human disease." (42 C.F.R. §72.25(a)(1)) Recombinant research and the commercial use of recombinant technology pose an even greater risk that the public will be exposed to infectious agents than does transportation. The same risk of communicable disease which gives the Secretary the authority to regulate the transportation of recombinant materials under §361 gives him the authority to regulate all recombinant DNA activities.

V. Relief

By this petition EDF and NRDC seek the following relief:

1. A legislative-type hearing to develop a policy on recombinant DNA research and technology.

2. Regulations binding on all parties conducting recombinant DNA research or otherwise engaged in recombinant DNA technology.

1/ §72.25 applies to microorganisms listed in subsection (C) which includes most microorganisms used in recombinant DNA research such as *E. coli*, Simian Viruses, Salmonella.

3. As interim relief, regulations which make the NIH guidelines binding on all parties engaged in recombinant DNA research and technology.

This relief is necessary to insure that the public has an adequate opportunity to participate in the decision of whether and under what conditions recombinant DNA research and technology should be permitted and to insure that the protection provided the public by the NIH guidelines is immediately extended through the application of the NIH guidelines to all recombinant DNA research and technology.

A. The Need for a Legislative-Type Hearing

The NIH guidelines, which at present are the only statement of government policy on recombinant DNA research and technology, are the product of the deliberations of scientists who are now conducting recombinant DNA research. The NIH guidelines had their origin in the Asilomar Conference held in Pacific Grove, California in February 1975. Many of the participants at that conference were the foremost molecular biologists from all over the world. The NIH Recombinant DNA Molecule Program Advisory Committee translated the recommendations of that conference into concrete proposals which became the NIH guidelines. The first opportunity the public had to participate in the regulation of recombinant research was in February of 1976 when the draft guidelines were released for public comment, and the Advisory Committee to the Director of NIH[1/] held an open meeting.

1/This committee should not be confused with the NIH Recombinant DNA Molecule Program Advisory Committee, which drafted the guidelines, but is one assembled early in 1976 from representatives of science, law, teaching, public interest groups, students, etc. to advise the director of NIH on the correctness or shortcomings of its efforts to regulate recombinant DNA research.

Although this meeting was not well publicized, many scientists, public interest groups and laymen were invited to attend and to comment on the guidelines.[2/] Additional input was sought from these same individuals during the two-month period following this meeting. A considerable body of material was received by commentators by the office of the Director of NIH, and is summarized, in part, in the Decision of the Director, NIH, to Release Guidelines for Research on Recombinant DNA Molecules (see 41 Fed. Reg. No. 131, pp. 27902-27911, July 7, 1976)

Little discussion was devoted to whether or not these experiments ought to be performed at all, even though the question was raised both by concerned laymen and by prominent scientists. That there is an intrinsic and even necessary good in recombinant DNA research has been a tacit assumption on the part of the NIH advisory committee which drafted the guidelines from the onset of its deliberations. We believe that this is, at least in part, a reflection of the fact that many of the committee members are now doing recombinant DNA research and have a vested interest in its future. In the public meeting held on February 9-10, 1976, the request was made that such potentially hazardous research should at least await the development of a strain of bacteria which is not a ubiquitous inhabitant of the human colon. E. coli is the current organism of choice simply because a large body of genetic information exists concerning this bacterium. This

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2/ A copy of the comments submitted by EDF at that time are attached as Appendix 1.

request was denied in an administrative decision by the director of NIH and not even submitted to the advisory committee for further debate in its April 1-2, 1976 meeting in which final revisions of the guidelines were made. At this meeting, all of the outside comments had been distilled down to ten typewritten pages of questions for the consideration of the recombinant DNA advisory committee, the same committee which had drafted the working version prepared early in 1976. Except for relatively minor changes in wording, the committee dealt summarily with the questions from the public, and the final version of the guidelines did not differ significantly from the version prepared prior to public input.

The legislative-type hearing should consider the following issues which were not adequately considered in the NIH proceedings which led to the promulgation of the guidelines:

(a) Whether or not recombinant DNA research on <u>any</u> level should be permitted at this time in view of our present state of knowledge.

(b) If some areas are to be permitted, what are they and what precautions are necessary to adequately protect the public and the environment? For example, what degree of physical containment should be considered adequate in light of human fallibility?

(c) Whether or not a strain of bacteria should be sought and studied to replace E. coli as the subject of most recombinant DNA experiments before this work be allowed to proceed.

(d) Whether or not an "ordinary" or normal, non-hazardous gene from one organism might become dangerous if expressed in the wrong place and wrong time in the wrong organism (this important question was virtually ignored by the advisory committee).

A legislative-type hearing conducted by HEW is the best forum for full consideration of the issues raised by recombinant DNA research and technology. In effect, such a hearing would amount to a broad-based public review of the existing NIH guidelines and would permit open debate on issues given little or no attention by the NIH Drafting Committee or the office of the director. Whether the activity is transportation of recombinant DNA materials, research, commercial production or use in the environment, HEW has the authority to regulate corporations and scientists whether or not they receive federal research support. Therefore, it is highly appropriate for HEW to hold such a hearing.

B. Final Regulations Governing All Parties Engaged

Promulgation of the NIH guidelines reflects a consensus that recombinant DNA research and technology pose a sufficient hazard to the public health and the environment to require the prohibition of some experiments and the imposition of safety

procedures for others. The hazards of recombinant DNA research and technology are no different if the research is being conducted by scientists employed by private corporations rather than the NIH. The risk that necessitated regulation of NIH grantees necessitates regulation of other research and technology. The need for regulation of all parties conducting recombinant DNA research is particularly great because even one release of a hazardous genetically altered bacterium, virus or plasmid could cause widespread illness or disruption of the environment.

C. Interim Relief

During the period before the hearing is held and final regulations are promulgated the public will be exposed to the potential hazards of recombinant DNA research and technology not now subject to NIH guidelines. Individuals who do not receive NIH grants or work for NIH are not effectively restrained from conducting any of the experiments which NIH deemed so dangerous that they should not be conducted at all. Nor are scientists not now covered by the guidelines required to practice physical and biological containment of organisms with recombinant DNA molecules. To protect the public until final regulations are promulgated, EDF and NRDC request that the Secretary immediately promulgate regulations which make the NIH guidelines binding on all parties engaged in recombinant DNA research and technology.

Respectfully submitted,

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